News

US government agency to investigate FDA over rofecoxib

Jeanne Lenzer *New York*

The US Government Accountability Office, a regulatory watchdog on federal government spending, is to investigate claims that the Food and Drug Administration attempted to silence one of its senior medical officers when he tried to warn that rofecoxib (Vioxx) caused heart attacks and strokes.

The drug was withdrawn on 30 September by its manufacturers, Merck, after a study found a fourfold increase in serious thromboembolic adverse events in patients receiving rofecoxib compared with patients receiving placebo (*BMJ* 2004;329:816, 9 Oct).

David Graham, associate director for science in the FDA Drug Center's Office of Drug Safety, said that he was subjected to "veiled threats" when he sent his report to superiors at the FDA, who wanted him to water down his findings.

The Government Accountability Office has already launched a separate investigation into the FDA after another FDA expert, Andrew Mosholder, said his report warning of the risks of antidepressants for children was suppressed (*BMJ* 2004;329:307, 7 Aug).

A spokesperson for the Government Accountability Office told the *BMJ* that it will now include Dr Graham's charges in their investigation and the agency will focus on the FDA's "handling of drug safety issues." The full scope of the investigation has not yet been determined, however, since "events continue to unfold," said the spokesperson.

Senator Chuck Grassley of Iowa said in a news release that the FDA's attempts to silence Dr Graham led to the FDA sitting "on the sidelines while life threatening issues threaten the American public."

In a letter of 15 October to the FDA, Mr Grassley asked, "Did the government agency that's supposed to regulate pharmaceuticals have an inappropriate agreement with Merck? And did a cosy relationship between the FDA and a pharmaceutical company allow a drug with known safety risks to stay on the market longer than it should have?"

Eric Topol, chief of cardiovascular medicine at the Cleveland Clinic, Ohio, said that the FDA took a passive approach: "They were the first ones to uncover the issue. They knew about this as early as November 18, 1999, when the data and safety monitoring board alerted Merck there was a serious problem. They could have ordered a large trial but they didn't. As a result, anywhere from 20 000 to 160 000 people suffered heart attacks and strokes."

MIKE DERER/AP

When David Graham of the FDA warned about the side effects of rofecoxib (Vioxx), he says he was subjected to "veiled threats"

The FDA responded to the *BMJ* with an email stating, "There was absolutely no undue pressure on Dr Graham. As a scientific agency, FDA values open discussion… the standard agency review process and procedure is a more rigorous peer review."

Mr Grassley provided evidence of what he called the "cosy relationship" between the FDA and Merck by releasing a copy of an email from 12 August from Anne Trontell, deputy director of the FDA's Office of Drug Safety, in which she criticises Dr Graham's report and wrote that the FDA should notify Merck before Dr Graham's review became public "so they can be prepared for extensive media attention that this will likely provoke." □

Pfizer criticised over delay in admitting drug's problems

Jeanne Lenzer *New York*

Pfizer delayed announcing negative data about its painkiller valdecoxib (Bextra), Curt Furberg, a member of the US Food and Drug Administration's Data Safety and Risk Management Advisory Committee, told the *BMJ* this week. When the company eventually presented its data to the FDA, it also left out important details, Dr Furberg alleges.

Pfizer stood to gain by Merck's withdrawal of rofecoxib on 30 September, after reports linked the drug to increased heart attacks and strokes (*BMJ* 2004;329:816, 9 Oct). That gain was amplified when a major health insurer, BlueCross BlueShield, announced that they had added valdecoxib to their formulary after the withdrawal of rofecoxib.

Pfizer initially defended valdecoxib, saying the drug was safe in patients with osteoarthritis and rheumatoid arthritis. But on 15 October the company issued a news release, qualifying its earlier statement. The release said, "In two trials in a high-risk surgery known as coronary artery bypass graft (CABG), an increase in cardiovascular events was observed in patients receiving Bextra" (www.pfizer.com).

That news, said Dr Furberg, a member of the FDA's Data Safety and Risk Management Advisory Committee, should have been released earlier. Dr Furberg asked Pfizer, after the withdrawal of rofecoxib, to supply him with data regarding the cardiovascular effects of valdecoxib. "I was struck by what they excluded," he told the *BMJ*. "They did not mention either of two trials of cardiac surgery patients."

The first of the two trials was published but in a manner that obscured the risks, according to Dr Furberg. He said, "They listed each [adverse] event individually and said the numbers were too small to analyse. But I added up heart attacks, strokes, and deaths and found a statistically significant fourfold increase over placebo." □